

**What is claimed is:**

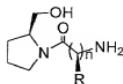
5 1. A method of treating a subject afflicted with an  
infection caused by vancomycin resistant Gram-  
positive bacteria in which resistance results from  
the conversion of an amide bond to an ester bond in  
the cell wall peptide precursors of the bacteria  
10 which comprises administering to the subject an  
antibacterial amount of vancomycin or a homolog of  
vancomycin and an amount of an agent effective to  
selectively cleave said ester bond so as to thereby  
treat the subject.

15 2. The method of claim 1, wherein the subject is a human  
being.

20 3. The method of claim 1, wherein the agent is an  
activated nucleophile, and is further characterized  
by the presence within the agent of an electrophile  
and chirality complementary to a bacterial cell wall  
depsipeptide.

25 4. The method of claim 1, wherein the agent is  
represented by the formula S-Pro-C<sub>n</sub>.

5. The method of claim 1, wherein the agent has the  
structure:



35 wherein n is an integer from 1 to 6 inclusive and R

is hydrogen or a C<sub>1</sub> to C<sub>6</sub> straight chain or branched alkyl group.

6. The method of claim 1, where the agent catalytically  
5 cleaves said ester bond.

7. The method of claim 1, wherein said ester bond is  
present in the structure D-Ala-D-Lac.

10 8. The method of claim 1, wherein the agent is  
administered prior to administering vancomycin or the  
homolog of vancomycin.

15 9. The method of claim 8, wherein the agent is  
administered a sufficient period of time prior to  
administering vancomycin or the homolog of vancomycin  
to permit cleavage of said ester bond to be effected.

20 10. The method of claim 1, wherein the agent and  
vancomycin or the homolog of vancomycin are  
administered simultaneously.

25 11. The method of claim 10, wherein the agent is  
covalently attached to vancomycin or the homolog  
of vancomycin.

12. The method of claim 1, wherein the bacteria are Van  
A, Van B, Van D or Van G Gram positive bacteria.

30 13. The method of claim 1, wherein the bacteria are  
Staphylococcus bacteria.

14. The method of claim 12, wherein the bacteria are S. aureus bacteria.

15. The method of claim 1, wherein the bacteria are Enterococcus bacteria.

16. The method of claim 1, wherein the bacteria are Streptococcus bacteria.

10 17. The method of claim 1, wherein the bacteria are Leuconostoc bacteria.

18. The method of claim 1, wherein the bacteria are Pediococcus bacteria.

15 19. The method of claim 1, wherein the bacteria are Lactobacillus bacteria.

20 20. The method of claim 1, wherein the bacteria are Erysipelothrix bacteria.

21. A method of killing vancomycin resistant Van A, Van B, Van D, or Van G Gram-positive bacteria which comprises contacting the bacteria with an agent that 25 selectively cleaves D-Ala-D-Lac cell wall depsipeptides in the bacteria in an amount effective to cleave such depsipeptides and an antibacterial amount of vancomycin or a homolog of vancomycin so as to thereby kill the bacteria.

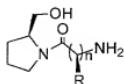
30 22. The method of claim 21, wherein the agent is an activated nucleophile, and is further characterized by the presence within the agent of an electrophile

and chirality complementary to a bacterial cell wall depsipeptide.

23. The method of claim 21, wherein the agent is  
5 represented by the formula S-Pro-Cn.

24. The method of claim 21, wherein the agent has the  
structure:

10



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wherein n is an integer from 1 to 6 inclusive and R  
is hydrogen or a C<sub>1</sub> to C<sub>6</sub> straight chain or branched  
alkyl group.

25. The method of claim 21, where the agent catalytically  
cleaves said ester bond.

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26. The method of claim 21, wherein said ester bond is  
present in the structure D-Ala-D-Lac.

25

27. The method of claim 21, wherein the agent is  
administered prior to administering vancomycin or the  
homolog of vancomycin.

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28. The method of claim 27, wherein the agent is  
administered a sufficient period of time prior to  
administering vancomycin or the homolog of vancomycin  
to permit cleavage of said ester bond to be effected.

29. The method of claim 21, wherein the agent and  
vancomycin or the homolog of vancomycin are

administered simultaneously.

30. The method of claim 29, wherein the agent is  
covalently attached to vancomycin or the homolog of  
5 vancomycin.

31. The method of claim 21, wherein the bacteria are  
Staphylococcus bacteria.

10 32. The method of claim 31, wherein the bacteria are S.  
aureus bacteria.

15 33. The method of claim 21, wherein the bacteria are  
Enterococcus bacteria.

34. The method of claim 21, wherein the bacteria are  
Streptococcus bacteria.

20 35. A method for determining whether a test compound  
selectively cleaves an ester bond present between two  
amino acid-like moieties in a depsipeptide which  
comprises contacting a compound comprising the  
structure X-Y, wherein each of X and Y are amino  
acid-like moieties and - is an ester bond with the  
25 test compound and determining whether the test  
compound cleaves the ester bond.

36. The method of claim 35, wherein the compound  
comprises the structure D-Ala-D-Lac.

30 37. The method of claim 35, wherein the compound  
comprises the structure L-(X-Y) wherein (X-Y) is D-  
Ala-D-Lac, and wherein L is a detectable label.

38. The method of claim 37, wherein the detectable label is a dye.

5 39. The method of claim 35, wherein the test compound is bound to a solid support.

40. The method of claim 35, wherein the test compound is present in a collection of compounds containing  
10 nucleophiles.

41. The method of claim 40, wherein the collection of compounds is a combinatorial library of compounds.

15 42. A method of treating a subject afflicted with an infection caused by glycopeptide antibiotic resistant Gram-positive bacteria in which resistance results from the conversion of an amide bond to an ester bond in the cell wall peptide precursors of the bacteria  
20 which comprises administering to the subject an antibacterial amount of a glycopeptide antibiotic and an amount of an agent effective to selectively cleave said ester bond so as to thereby treat the subject.

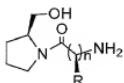
25 43. The method of claim 42, wherein the subject is a human being.

44. The method of claim 42, wherein the agent is an activated nucleophile, and is further characterized  
30 by the presence within the agent of an electrophile and chirality complementary to a bacterial cell wall depsipeptide.

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45. The method of claim 42, wherein the agent is represented by the formula S-Pro-C<sub>n</sub>.

46. The method of claim 42, wherein the agent has the 5 structure:



wherein n is an integer from 1 to 6 inclusive and R is hydrogen or a C<sub>1</sub> to C<sub>6</sub> straight chain or branched alkyl group.

15 47. The method of claim 42, where the agent catalytically cleaves said ester bond.

48. The method of claim 42, wherein said ester bond is present in the structure D-Ala-D-Lac.

20 49. The method of claim 42, wherein the agent is administered prior to administering the glycopeptide antibiotic.

25 50. The method of claim 49, wherein the agent is administered a sufficient period of time prior to administering the glycopeptide antibiotic to permit cleavage of said ester bond to be effected.

30 51. The method of claim 42, wherein the agent and the glycopeptide antibiotic are administered simultaneously.

52. The method of claim 51, wherein the agent is covalently attached to the glycopeptide antibiotic.

53. The method of claim 42, wherein the bacteria are Staphylococcus bacteria.

54. The method of claim 53, wherein the bacteria are S. aureus bacteria.

10 55. The method of claim 42, wherein the bacteria are Enterococcus bacteria.

56. The method of claim 42, wherein the bacteria are Streptococcus bacteria.

15 57. The method of claim 42, wherein the bacteria are Leuconostoc bacteria.

58. The method of claim 42, wherein the bacteria are Pediococcus bacteria.

20 59. The method of claim 42, wherein the bacteria are Lactobacillus bacteria.

25 60. The method of claim 42, wherein the bacteria are Erysipelothrix bacteria.

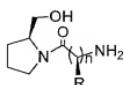
30 61. A method of killing glycopeptide antibiotic resistant Gram-positive bacteria which comprises contacting the bacteria with an agent that selectively cleaves D-Ala-D-Lac cell wall depsipeptides in the bacteria in an amount effective to cleave such depsipeptides and

an antibacterial amount of the glycopeptide antibiotic so as to thereby kill the bacteria.

62. The method of claim 61, wherein the agent is an  
5 activated nucleophile, and is further characterized  
by the presence within the agent of an electrophile  
and chirality complementary to a bacterial cell wall  
depsipeptide.

10 63. The method of claim 61, wherein the agent is  
represented by the formula S-Pro-Cn.

15 64. The method of claim 61, wherein the agent has the  
structure:



20 wherein n is an integer from 1 to 6 inclusive and R  
is hydrogen or a C<sub>1</sub> to C<sub>6</sub> straight chain or branched  
alkyl group.

25 65. The method of claim 61, where the agent catalytically  
cleaves said ester bond.

66. The method of claim 61, wherein said ester bond is  
present in the structure D-Ala-D-Lac.

30 67. The method of claim 61, wherein the agent is  
administered prior to administering the glycopeptide  
antibiotic.

5           68. The method of claim 61, wherein the agent is administered a sufficient period of time prior to administering the glycopeptide antibiotic to permit cleavage of said ester bond to be effected.

10           69. The method of claim 67, wherein the agent and the glycopeptide antibiotic are administered simultaneously.

15           70. The method of claim 61, wherein the agent is covalently attached to the glycopeptide antibiotic.

71. The method of claim 69, wherein the bacteria are Staphylococcus bacteria.

15           72. The method of claim 61, wherein the bacteria are S. aureus bacteria.

20           73. The method of claim 71, wherein the bacteria are Enterococcus bacteria.

74. The method of claim 61, wherein the bacteria are Streptococcus bacteria.

25           75. The method of claim 61, wherein the bacteria are Leuconostoc bacteria.

76. The method of claim 61, wherein the bacteria are Pediococcus bacteria.

30           77. The method of claim 61, wherein the bacteria are Lactobacillus bacteria.

78. The method of claim 61, wherein the bacteria are Erysipelothrix bacteria.

5 79. The method of claim 21, wherein the bacteria are Leuconostoc bacteria.

80. The method of claim 21, wherein the bacteria are Pediococcus bacteria.

10 81. The method of claim 21, wherein the bacteria are Lactobacillus bacteria.

82. The method of claim 21, wherein the bacteria are Erysipelothrix bacteria.